

**WHAT IS CLAIMED IS:**

1. A method of treating mammalian cancer or hyperproliferative cells, said method comprising contacting said cells with a tumor suppressor protein or tumor suppressor nucleic acid and also contacting said cell with at least one adjunctive anti-cancer agent.
2. The method of claim 1, wherein said adjunctive anti-cancer agent is a microtubule affecting agent.
3. The method of claim 2 wherein said microtubule affecting agent is paclitaxel or a paclitaxel derivative.
4. The method of claim 1, wherein said method further comprises contacting a cell with a chemotherapeutic agent.
5. The method of claim 4, wherein said chemotherapeutic agent is cisplatin, carboplatin, or navelbine.
6. The method of claim 1, wherein said tumor suppressor nucleic acid is a nucleic acid that encodes a tumor suppressor protein selected from the group consisting of a wild-type p53 protein, and a retinoblastoma (RB) protein.
7. The method of claim 6, wherein said tumor suppressor nucleic acid encodes a wild-type p53 protein.
8. The method of claim 6, wherein said retinoblastoma protein is a p110<sup>RB</sup> or a p56<sup>RB</sup>.
9. The method of claim 1, wherein said nucleic acid is delivered by a vector selected from the group consisting of a naked DNA plasmid, a plasmid within a

liposome, a plasmid complexed with a lipid, a viral vector, an AAV vector, and a recombinant adenoviral vector.

10. The method of claim 1, wherein said nucleic acid is delivered by a recombinant adenoviral vector.

11. The method of claim 10, wherein said nucleic acid is delivered by a recombinant adenoviral vector comprising a partial or total deletion of a protein IX DNA and comprising a nucleic acid encoding a wild-type p53 protein.

12. The method of claim 11, wherein said deletion of the protein IX gene sequence extends from about 3500 bp from the 5' viral termini to about 4000 bp from the 5' viral termini.

13. The method of claim 12, further comprising deletion of a non-essential DNA sequence in adenovirus early region 3.

14. The method of claim 11, further comprising deletion of a non-essential DNA sequence in adenovirus early region 4.

15. The method of claim 11, further comprising a deletion of DNA sequence designated E1a and E1b.

16. The method of claim 10, wherein said recombinant adenoviral vector comprises the adenovirus type 2 major late promoter or the human CMV promoter, the adenovirus type 2 tripartite leader cDNA and a human p53 cDNA.

17. The method of claim 16, wherein said vector is A/C/N/53.

18. The method of claim 2, wherein said microtubule affecting agent is selected from the group consisting of paclitaxel and Taxotere®.

19. The method of claim 18, wherein said microtubule affecting agent is Taxol®.

20. The method of claim 3, wherein said cells are first contacted with said tumor suppressor nucleic acid or tumor suppressor protein and is subsequently contacted with said paclitaxel or paclitaxel derivative.

21. The method of claim 3, wherein said cells are first contacted with said paclitaxel or paclitaxel derivative and subsequently contacted with said tumor suppressor protein or tumor suppressor nucleic acid.

22. The method of claim 2, wherein said cells are simultaneously contacted with said paclitaxel or paclitaxel derivative and with said tumor suppressor protein or tumor suppressor nucleic acid.

23. The method of claim 1, wherein said cells are neoplastic cells.

24. The method of claim 23, wherein said neoplastic cells comprise a cancer selected from the group consisting of an ovarian cancer, pancreatic cancer, a non-small cell lung cancer, small cell lung cancer, hepatocarcinoma, melanoma, retinoblastoma, breast tumor, colorectal carcinoma, leukemia, lymphoma, brain tumor, cervical carcinoma, sarcoma, prostate tumor, bladder tumor, tumor of the reticuloendothelial tissues, Wilm's tumor, astrocytoma, glioblastoma, neuroblastoma, osteosarcoma, renal cancer, and head and neck cancer.

25. The method of claim 1, wherein said tumor suppressor protein or tumor suppressor nucleic acid is dispersed in a pharmacologically acceptable excipient.

26. The method of claim 3, wherein said paclitaxel or paclitaxel derivative is dispersed in a pharmacologically acceptable excipient.

27. The method of claim 2, wherein said tumor suppressor protein or tumor suppressor nucleic acid and said paclitaxel or paclitaxel derivative are dispersed in a single composition.

28. The method of claim 1, wherein said contacting comprises injecting said tumor suppressor protein or tumor suppressor nucleic acid into a tumor.

29. The method of claim 1, wherein said contacting comprises intra-arterial injection of said tumor suppressor protein or tumor suppressor nucleic acid.

30. The method of claim 29, wherein said contacting is selected from the group consisting of intra-hepatic artery injection of said tumor suppressor protein or tumor suppressor nucleic acid for the treatment of liver cancer and intraperitoneal administration of said tumor suppressor protein or tumor suppressor nucleic acid for the treatment of ovarian cancer.

31. The method of claim 3, wherein said contacting comprises injecting said paclitaxel or paclitaxel derivative into a tumor.

32. The method of claim 3, wherein said contacting comprises intravenously injecting said paclitaxel or paclitaxel derivative.

33. The method of claim 1, wherein said contacting comprises systemic, regional, local, topical, intraperitoneal, intra-pleural cavity, oral, buccal, sublingual, intra-tracheal, transmucosal, bladder, vaginal, uterine, rectal, or nasal administration.

34. The method of claim 2, comprising contacting said cells with A/C/N/53 and paclitaxel.

35. The method of claim 1, wherein said contacting cells with a tumor suppressor protein or tumor suppressor nucleic acid comprises contacting said cells with

said tumor suppressor protein or tumor suppressor nucleic acid in a multiplicity of treatments each separated by at least about 6 hours.

36. The method of claim 1, wherein said method comprises at least three treatments separated by about 24 hours.

37. The method of claim 1, wherein:

    said tumor suppressor protein or tumor suppressor nucleic acid is administered in a total dose ranging from about  $1 \times 10^9$  to about  $7.5 \times 10^{15}$  adenovirus particles in a treatment regimen selected from the group consisting of: the total dose in a single dose, the total dose divided over 5 days and administered daily, the total dose divided over 15 days and administered daily, and the total dose divided over 30 days and administered daily; and

    said paclitaxel or paclitaxel derivative is administered in a total dose ranging from about 75 to about  $350 \text{ mg/m}^2$  over 24 hours in a treatment regimen selected from the group consisting of administration in a single dose, in a dose administered daily on day 1 and day 2, in a dose administered daily on day 1, day 2, and day 3, on a daily dosage for 15 days, on a daily dosage for 30 days, on daily continuous infusion for 15 days, on daily continuous infusion for 30 days.

38. The method of claim 37, wherein said method is repeated for two or more cycles.

39. The method of claim 38, wherein said two or more cycles are spaced apart by three or four weeks.

40. The method of claim 38, wherein said method is repeated for three cycles.

41. A kit for the treatment of mammalian cancer or hyperproliferative cells, said kit comprising:

a first container comprising a tumor suppressor protein or nucleic acid selected from the group consisting of wild-type p53 protein or nucleic acid, or a retinoblastoma (RB) protein or nucleic acid; and  
a second container comprising at least one adjunctive anti-cancer agent.

42. The kit of claim 41, wherein said tumor suppressor nucleic acid encodes a wild-type p53 protein.

43. The kit of claim 41, wherein said adjunctive anti-cancer agent is paclitaxel or a paclitaxel derivative.

44. The kit of claim 41, further comprising instructions describing the administration of both said tumor suppressor protein or nucleic acid and said adjunctive anti-cancer agent to inhibit the growth or proliferation of said cell.

45. The kit of claim 41, wherein said tumor suppressor protein or tumor suppressor nucleic acid is selected from the group consisting of p53, p110<sup>RB</sup>, and p56<sup>RB</sup>.

46. The kit of claim 41, wherein said first container contains a nucleic acid that is contained in a recombinant adenoviral vector.

47. The kit of claim 46, wherein said nucleic acid is contained in a recombinant adenoviral vector comprising a partial or total deletion of a protein IX DNA and comprising a nucleic acid encoding a p53 protein.

48. The kit of claim 47, wherein said deletion of the protein IX gene sequence extends from about 3500 bp for the 5' viral termini to about 4000 bp from the 5' viral termini.

49. The kit of claim 48, further comprising a deletion of DNA sequence designated E1a and E1b.

50. The kit of claim 46, wherein said recombinant adenoviral vector comprises the adenovirus type 2 major late promoter or the human CMV promoter, the adenovirus type 2 tripartite leader cDNA and a human p53 cDNA.

51. The kit of claim 46, wherein said vector is A/C/N/53.

52. A pharmacological composition comprising a tumor suppressor protein or a tumor suppressor nucleic acid and at least one adjunctive anti-cancer agent.

53. The composition of claim 52, wherein said adjunctive anti-cancer agent is paclitaxel or a paclitaxel derivative.

54. The composition of claim 52, wherein said tumor suppressor protein or tumor suppressor nucleic acid is selected from the group consisting of a nucleic acid that encodes a wild-type p53 protein, a nucleic acid that encodes a retinoblastoma (RB) protein, a wild-type p53 protein, and a retinoblastoma (RB) protein.

55. The composition of claim 52, wherein said nucleic acid encodes a wild-type p53 protein.

56. The composition of claim 52, wherein said nucleic acid encodes a said retinoblastoma p110<sup>RB</sup> or a p56<sup>RB</sup>.

57. The composition of claim 52, wherein said nucleic acid is contained in recombinant adenoviral vector.

58. The composition of claim 57, wherein said nucleic acid is contained in a recombinant adenoviral vector comprising a partial or total deletion of a protein IX DNA and comprising a nucleic acid encoding a P53 protein.

59. The composition of claim 58, wherein said deletion of the protein IX gene sequence extends from about 3500 bp for the 5' viral termini to about 4000 bp from the 5' viral termini.

60. The composition of claim 59, further comprising a deletion of DNA sequence designated E1a and E1b.

61. The composition of claim 57, wherein said recombinant adenoviral vector comprises the adenovirus type 2 major late promoter or the human CMV promoter, the adenovirus type 2 tripartite leader cDNA and a human p53 cDNA.

62. The composition of claim 57, wherein said vector is A/C/N/53.

63. The composition of claim 53, wherein said paclitaxel or paclitaxel derivative is paclitaxel.

64. A composition comprising a mammalian cancer or hyperproliferative cell, wherein said cell contains an exogenous a tumor suppressor nucleic acid or a tumor suppressor protein and paclitaxel or a paclitaxel derivative.

65. The composition of claim 64, wherein said tumor suppressor nucleic acid is a nucleic acid that encodes a tumor suppressor protein selected from the group consisting of wild-type p53 protein, and a retinoblastoma (RB) protein.

66. The composition of claim 64, wherein said tumor suppressor nucleic acid encodes a wild-type p53 protein.

67. The composition of claim 65, wherein said retinoblastoma protein is a p110<sup>RB</sup> or a p56<sup>RB</sup>.

68. The composition of claim 64, wherein said cells are a present in a mammal.

69. The composition of claim 64, wherein said cells are neoplastic cells.

70. The composition of claim 69, wherein said neoplastic cells comprise a cancer selected from the group consisting of an ovarian cancer, pancreatic cancer, a non-small cell lung cancer, small cell lung cancer, hepatocarcinoma, melanoma, retinoblastoma, breast tumor, colorectal carcinoma, leukemia, lymphoma, brain tumor, cervical carcinoma, sarcoma, prostate tumor, bladder tumor, tumor of the reticuloendothelial tissues, Wilm's tumor, astrocytoma, glioblastoma, neuroblastoma, osteosarcoma, renal cancer, and head and neck cancer.

71. A method of treating a metastatic cell, said method comprising contacting said cell with a tumor suppressor nucleic acid or tumor suppressor polypeptide.

72. The method of claim 71, wherein said contacting comprises topical administration of a tumor suppressor nucleic acid to a surgical wound.

73. The method of claim 71, wherein said cells are further contacted with at least one adjunctive anti-cancer agent.

74. The method of claim 73, wherein said adjunctive anti-cancer agent is paclitaxel.

75. The method of claim 73, wherein said adjunctive anti-cancer agent is a microtubule affecting agent.

76. The method of claim 71, wherein said method further comprises contacting said cell with a chemotherapeutic agent.

77. The method of claim 76, wherein said chemotherapeutic agent is cisplatin, carboplatin, or navelbine.